ABSTRACTS

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Antiphospholipid antibodies and subsequent thrombo-occlusive events in patients with ischemic stroke

The APASS Investigators. JAMA 2004;291:576-84.

Conclusions: In patients with ischemic stroke, antiphospholipid antibodies (lupus anticoagulant [LA] or anticardiolipin antibody [aCL]) do not predict an increased risk for another thromboembolic or vascular occlusive event over 2 years, nor do they predict a differential response to warfarin or aspirin therapy.

Summary: This is a prospective study derived from participants in the warfarin versus aspirin recurrent stroke study (WARSS). The current study, the antiphospholipid antibodies and stroke study (APASS), tested hypotheses specified prior to initiation of the WARSS. The goal was to evaluate the effect of baseline antiphospholipid antibody positivity on late thrombo-occlusive events in patients with ischemic stroke. The main outcome measure was a 2-year rate of the composite end point of death from any cause, ischemic stroke, transient ischemic attack, myocardial infarction, deep venous thrombosis, pulmonary embolism, and other systemic thrombo-occlusive events. Analysis was done with respect to both aCL and LA levels.

There were 1,770 APASS patients. Of these, 720 (41%) were antiphospholipid antibody positive and 1,050 (59%) were negative. Positive antiphospholipid antibody status did not confer increased risk of thrombo-occlusive events during follow-up. This was true for patients treated with warfarin (relative risk [RR], 0.99; 95% confidence interval [CI], 0.75-1.31; $P = .94$) or aspirin (RR, 0.94; 95% CI, 0.70-1.28; $P = .71$). The overall composite end-point event rate in antiphospholipid antibody–positive patients was 22.2%; it was 21.8% among negative patients. Patients who were positive at baseline for both LA and aCL tended to have a higher event rate (31.7%) than did patients who tested negative for both LA and aCL (24.0%), (RR, 1.36; 95% CI, 0.97-1.92; $P = .07$). There were no specific LA tests, or aCL isotopes or titers, that conferred increased risk of thrombo-occlusive events.

Comment: Antiphospholipid antibodies are linked to an immune-mediated coagulopathy. The data here indicate no role for antiphospholipid antibodies in predicting subsequent vascular risk in patients with ischemic stroke or in predicting response to aspirin or warfarin therapy. By inference, the true role of antiphospholipid antibodies in patients with peripheral vascular disease probably still remains to be defined.

Inhibition of experimental abdominal aortic aneurysm in the rat by use of decoy oligodeoxynucleotides suppressing activity of nuclear factor kb and ets transcription factors

Nakashima H, Aokin M, Miyake T, et al. Circulation 2004;109:132-8.

Conclusion: The use of a chimeric decoy active against nf-kb and ets transcription factors inhibits progression of aneurysmal dilatation in a rat model of abdominal aortic aneurysm (AAA).

Summary: Matrix metalloproteinases (MMPs) lead to destruction of elastin and may play a role in aneurysm development and rupture. Transcription factor nuclear factor (nf)-kb regulates the transcription of MMP 1, 2, 3, and 9. The ets-1 family of transcription factors activates the transcription of genes coding MMP 1, 3, and 9. The authors developed a chimeric decoy oligodeoxynucleotide (ODN) to inhibit both nf-kb and ets transcription factors. The goal was to decrease aneurysmal degeneration in a rat model through delivery of ODN and subsequent inhibition of MMP expression.

AAAs were induced in rats by transient aortic profusion with elastase. Transfection of decoy ODN was performed by wrapping a delivery sheet containing ODN around the aorta. At 7 days, using a gel-mobility shift assay, both ets and nf-kb binding activities were inhibited by the decoy. Animals treated with the chimeric decoy ODN had significantly less progression of AAA enlargement at 4 weeks than control animals. This was accompanied by a reduction of MMP expression. Scrambled decoy ODN had no effect.

Comment: These data suggest a potentially important role in aneurysm development for transcription factors nuclear factor (nf)-kb and ets-1. The chimeric decoy is able to bind to free nf-kb and ets and thereby prevent activation of genes dependent upon these transcription factors. This is truly exciting research targeting inhibition of degenerative processes at the genetic level.

Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes

Saydah SH, Fradkin J, Cowie CC. JAMA 2004;291:335-42.

Conclusion: Only 7.3% of adults with diabetes meet recommended goals for hemoglobin (HbA1c) levels, blood pressure, and total cholesterol.

Summary: The American Diabetes Association (ADA) has standards of medical care for individuals with diabetes. The aim is to reduce vascular complications of diabetes. The ADA goal for glycemic control is HbA1c levels <7%. The goal for blood pressure control is a systolic pressure <130 mm Hg and a diastolic pressure <80 mm Hg. The national cholesterol education program adult treatment panel sets a goal of a total cholesterol level of <200 mg/dL.

The authors analyzed adults ≥age 20 years with known and previously diagnosed diabetes who had participated in 2 National Health and Nutrition Examination Surveys (NHANES). The first survey was conducted between 1988 and 1994 and the second from 1999 to 2000. In the latter survey, only 37% of participants achieved a target goal of HbA1c level <7%. Only 35.8% of participants achieved a target of a systolic blood pressure <130 mm Hg and a diastolic pressure <80 mm Hg. With respect to hemoglobin A1c levels and blood pressure control, there was no improvement from the 1988-1994 survey to the 1999-2000 survey. In the first NHANES survey 66.1% had a total cholesterol level >200 mg/dL, while in the second NHANES survey 51.8% had a total cholesterol >200 mg/dL, ($P < .001$). Overall, only 7.3% (95% confidence interval, 2.8-11.9) of adults in the second NHANES survey met recommended goals of HbA1c, blood pressure, and total cholesterol.

Comment: The study indicates that, despite widespread publicity regarding the importance of glycemic, lipid, and blood pressure control in patients with diabetes, the US health care system has not worked well to improve glycemic and blood pressure control in people with diabetes. While lipid levels have improved, they are still unacceptable. Clearly, further public health efforts are urgently needed to control risk factors for vascular disease among people with diabetes.

Does supervised exercise offer adjuvant benefit over exercise advice alone for the treatment of intermittent claudication? A randomized trial

Cheetham BR; Burgess L; Ellis N; et al. Eur J Vasc Endovasc Surg 2004; 27:17-23.

Conclusion: A weekly supervised exercise class for 6 months provides greater improvement in patient symptoms, walking distance, and quality of life than does written and verbal exercise advice alone.

Summary: The study consisted of 59 patients with intermittent claudication. The patients were randomized to receive just advice to exercise (n = 30), or to receive advice to exercise along with a once-a-week 45-minute supervised exercise/motivation class (n = 29). The patients were evaluated at baseline and at 6-month follow-up. Evaluation included a short-form quality of life questionnaire (SF-36), the Charing Cross symptom-specific claudication questionnaire (CCCQ), and treadmill walking distance at 3.5km/h with a 12% grade.

The mean age of the patients was 68 years. At 6-month follow-up, the supervised exercise group improved treadmill walking by 129%. The advice-alone group improved treadmill walking by 69% ($P = .001$). Improvement was maintained at 9- and 12- month assessments. There were no significant differences between the groups with regard to follow-up SF 36 scores compared with baseline. By 9 months the advice-only group's CCCQ score improved 16% from baseline while the supervised-exercise group had a 43% improvement over baseline ($P < .05$). At 6 months, the supervised-exercise group reported a higher frequency of 30-minute walks compared with the advice-only group.

Comment: The data indicate the power of continual reinforcement in a structured program to maximize the beneficial effects of exercise therapy in patients with intermittent claudication. Patients who undergo interventional or operative treatment of claudication are rarely normalized. It would be interesting to see if supervised exercise programs in patients who undergo angioplasty or surgery for claudication would also improve overall quality of life and walking distance over that achieved with intervention alone.

Transient Ischemic Attacks Before Ischemic Stroke: Preconditioning the Human Brain? A Multicenter Magnetic Resonance Imaging Study

Wegener S, Gottchalk B, Jobanobic B, et al. Stroke 2004;35:616-21.

Conclusion: Stroke patients with and without prodromal transient ischemic attacks (TIAs) have similar profusion lesions, but patients with prodromal transient ischemic attacks have smaller final infarct sizes, suggesting a neuroprotective effect of TIAs in patients with subsequent stroke.

Summary: The authors studied 65 patients with first-ever ischemic strokes who were admitted to 4 university hospitals in Germany. Patients were examined with diffusion and profusion weighted magnetic resonance